

## RESEARCH ARTICLE

# Endoscopic Submucosal Dissection Versus Endoscopic Mucosal Resection for the Treatment of Early Esophageal Carcinoma: a Meta-analysis

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## Abstract

Endoscopic submucosal dissection (ESD) was originally developed for en bloc resection of large, flat gastrointestinal lesions. Compared with endoscopic mucosal resection (EMR), ESD is considered to be more time consuming and have more complications for treatment of early esophageal carcinoma, such as bleeding, stenosis and perforation. The objective of this study was to compare the efficacy and safety of ESD and EMR for such lesions. We searched databases, such as PubMed, EMBASE, Cochrane Library and Science Citation Index updated to 2013 for related trials. In the meta-analysis, the main outcome measurements were the en bloc resection rate, the histologically resection rate and the local recurrence rate. We also compared the operation time and the incidences of procedure-related complications. Five trials were identified, and a total of 710 patients and 795 lesions were included. The en bloc and histologically complete resection rates were higher in the ESD group compared with the EMR group (odds ratio (OR) 27.3; 95% CI, 11.5-64.8; OR 18.4; 95% CI, 8.82-38.59). The local recurrence rate was lower in the ESD group (OR 0.13, 95% CI 0.04-0.43). The meta-analysis also showed ESD was more time consuming, but did not increase the complication rate ( $P=0.76$ ). The results implied that compared with EMR, ESD showed better en bloc and histologically resection rates, and lower local recurrence, without increasing the incidence of procedure-related complications in the treatment of early esophageal carcinoma.

**Keywords:** Endoscopic submucosal dissection - endoscopic mucosal resection - early esophageal carcinoma

*Asian Pac J Cancer Prev*, 15 (4), 1803-1806

## Introduction

Early esophageal carcinoma includes mucosal and submucosal carcinomas with or without the presence of lymph node metastasis. The prognosis is good after surgery (Chen et al., 2013). To those without lymph node metastasis, endoscopic resection, such as EMR and ESD, has been suggested as alternatives to esophagectomy in the treatment of these lesions, the effect can be matched with surgery (Inoue et al., 2010).

EMR is widely accepted because of its minimal invasion, low cost, good patients' tolerance, and better patient quality of life after operation, but larger lesions are hard to be resected completely (Tada, 1993). ESD, which had a significantly higher rate of histologically complete resection and local recurrence, was developed to solve the problems (Bialek et al., 2013). However, the operation time is longer and the complication rate is higher for ESD than EMR.

There is no current consensus on the optimal endoscopic method for the treatment of early esophageal carcinoma. We performed a meta-analysis to compare the efficacy and safety of EMR and ESD for the treatment of early esophageal carcinoma.

## Materials and Methods

### Search strategy

Databases including PubMed, EMBASE, the Cochrane Library, and Science Citation Index updated to August 2013 to identify related articles in English language that compared EMR and ESD were searched by us. All bibliographies were indentified in the reference list. The searching terms were "EMR or endoscopic mucosal resection" and "ESD or endoscopic submucosal dissection". Major proceedings of international meetings (such as Digestive Disease Week, Asian Pacific Digestive Week, and so on) were also hand-searched.

### Study selection

The inclusion and exclusion criteria are shown in Table 1.

### Data extraction

Data were extracted by one investigator and confirmed by the other according to a predefined data extraction form. Disagreements were resolved by consultation with a third investigator. The following data were collected: year of publication, first author, country, duration, number of

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**Table 1. The Inclusion and Exclusion Criteria**

Inclusion criteria	Exclusion criteria
Early esophageal carcinoma diagnosis for every patient has been confirmed by histology.	Case report.
Comparison of EMR and ESD for the treatment of early esophageal carcinoma.	Comment.
Written in English.	Review.
	Letter to editor.
	Insufficient data.
	Guidelines.

**Table 2. The Key Characteristics of the Included Studies**

Year of publication	First author	Country	Duration	Patients	Lesions	Mean age	Tumor size (mm)
2008	Ishihara R	Japan	2002.1-2007.10	ESD 29 EMR 119	ESD 31 EMRC 68 2-channel EMR 72	ESD 64 EMRC 65 2-channel EMR 64	ESD 16±4; EMRC 13±4; 2-channel EMR 12±5
2010	Takahashi H	Japan	1994.3-2007.07	ESD 116 EMR184	ESD 116 EMR 184	ESD 67.1 EMR 66.4	ESD 30±16; EMR 20±11.
2010	Teoh AY	China	2002.1-2007.12	ESD 18 EMR 10	ESD 22 EMR 13	ESD 67.5 EMR 61	ESD 24.3±9.8; EMR 11.5±3.5.
2011	Urabe Y	Japan	2005.10-2009.3	ESD 59 EMR 63	ESD 79 EMR 83	ESD 65.3 EMR 63.8	Not mentioned.
2011	Yamashita T	Japan	1997.1-2009.12	A total of 112	ESD 71 EMR 56	Not mentioned	ESD 21.3±11.1; EMR 19.4±11.2

participants and lesions in each group, age, tumor size and endpoints (en bloc resection rate, histologically complete resection rate, operation time, complications and local recurrence rate).

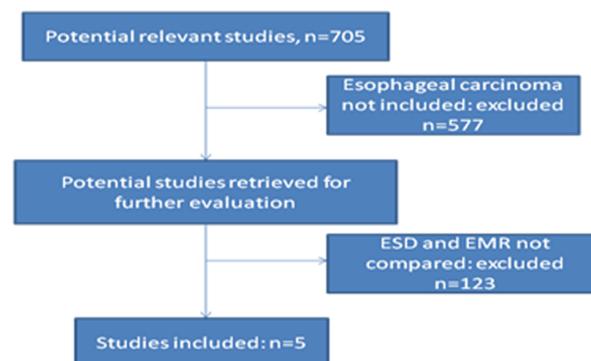
*Statistical analysis*

All data extracted were entered in the freeware program Review Manager (Version 5.0 for Windows, Cochrane Collaboration). The weighted mean difference was recommended for continuous data, and the odds ratio (OR) with 95% confidence intervals (CI) was recommended for dichotomous data. Statistical heterogeneity between trials was evaluated by the chi-square test and was considered to be present when *P* less than 0.1. We also used *I*<sup>2</sup> to assess the heterogeneity. *I*<sup>2</sup> more than 50% was considered to be statistical significance. In the absence of statistically significant heterogeneity, only the OR by the fixed effect model is given in the results. In the presence of statistical heterogeneity, heterogeneity was explored by subgroup analysis or a random-effects model.

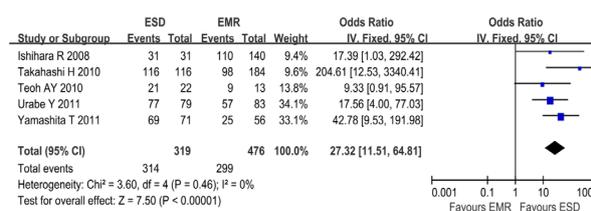
**Results**

*Study selection*

A total of 705 potential studies were retrieved for the meta-analysis, 577 were excluded for not including the esophageal carcinoma. 123 were excluded because EMR and ESD were not compared. The remaining 5 eligible studies (Iishi et al., 2008; Takahashi et., 2010; Teoh et al., 2010; Urabe et al., 2011; Yamashita et al., 2011) were chosen for further analysis (Figure 1). A total of 795 lesions were included in the meta-analysis, including 319 lesions in the ESD group and 476 lesions in the EMR group. All of the studies were respective case-control studies, not randomized controlled trials (RCTs). The key characteristics of the studies are listed in Table 2.



**Figure 1. Flow Diagram of Trial Selection**



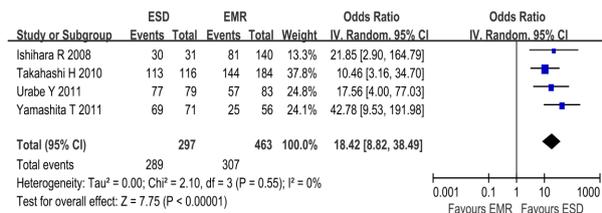
**Figure 2. En Bloc Resection Rate Comparing ESD and EMR**

*En bloc resection rate*

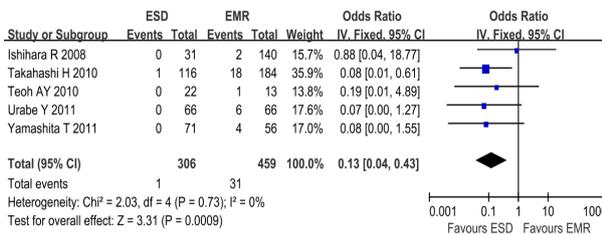
The en bloc resection rate was reported in all of the 5 studies. No heterogeneity was detected in the 5 studies (*P* = 0.46; *I*<sup>2</sup> = 0%), a fixed effect model was applied. The analysis showed a higher en bloc resection rate in the ESD group (314/319) than in the EMR group (299/476) (OR 27.32; 95% CI, 11.51-64.81) (Figure 2).

*Histologically resection rate*

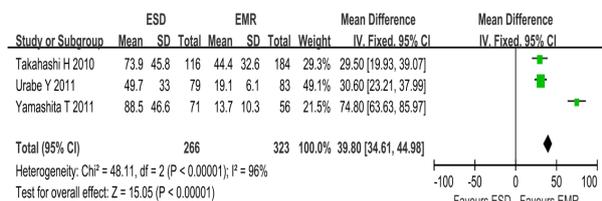
In the present 5 studies, the histologically resection rate was reported. There was heterogeneity among the studies (*P* = 0.02, *I*<sup>2</sup> = 65%). We excluded the study with the smallest samples (8), and the heterogeneity was eliminated



**Figure 3. Histologically Complete Resection Rate Comparing ESD and EMR**



**Figure 4. Local Recurrence Rate Comparing ESD and EMR**



**Figure 5. Procedural Time Comparing ESD and EMR**

( $P = 0.55$ ;  $I^2 = 0\%$ ). A fixed effect model was applied, the subsequent analysis showed the histologically resection rate was significantly higher in the ESD group (289/297) than in the EMR group (307/463) (OR 18.42; 95% CI, 8.82-38.49) (Figure 3).

#### Local recurrence rate

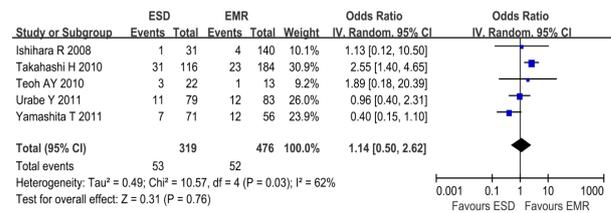
All of the studies reported the local recurrence after operation. Because there was no heterogeneity in the studies ( $P = 0.73$ ,  $I^2 = 0\%$ ), a fixed effect model was applied. Data showed the local recurrence rate was higher in the EMR group (31/459) than in the ESD group (1/306) (OR 0.13, 95% CI 0.04-0.43) (Figure 4).

#### Procedural time

Three studies (Teoh et al., 2010; Urabe et al., 2011; Yamashita et al., 2011) compared the operation time between the two groups. A random-effect model was applied because of the heterogeneity ( $P < 0.00001$ ,  $I^2 = 96\%$ ). Longer time was needed in the ESD group than in the EMR group (Figure 5).

#### Procedure-related complications

Data for procedure-related complications were reported in all of the studies included. There was heterogeneity among the studies ( $P = 0.03$ ,  $I^2 = 62\%$ ). The meta-analysis demonstrated that the complication rate occurred in 16.9% of the ESD group (53/319) versus 13.6% of the EMR group (52/476) (OR 1.14; 95% CI, 0.5-2.62) (Figure 6). We ruled out the study from China (Teoh AY et al., 2010), heterogeneity still existed ( $P < 0.01$ ,  $I^2 = 71\%$ ).



**Figure 6. Procedure-related Complications Comparing ESD and EMR**

## Discussion

In the present analysis, 5 retrospective studies were included, the results confirmed ESD showed higher rates for en bloc resection and histologically complete resection of the lesions than EMR. Local recurrence rate was lower in the ESD group without increasing the risk of complications. On the other hand, ESD is more time-consuming may be attributed to the complex procedure and more time is needed to stop bleeding during operation.

EMR is an endoscopic technique designed for removal of sessile or flat neoplasms confined to the superficial layers (mucosa and submucosa) of the gastrointestinal tract and is typically used for removal of lesions smaller than 2 cm or piecemeal removal of larger lesions (ASGE TECHNOLOGY COMMITTEE et al., 2008). For large lesions, incomplete resection is common, which can lead to local recurrence. ESD is a newly developed and epoch-making method, which has been developed for en bloc removal of large (usually larger than 2 cm), flat gastrointestinal tract lesions. The shortcomings of ESD were more time-consuming, higher rate of procedure related complications and more costly (Ohkuwa et al., 1988; Hirao et al., 1998; Yamamoto et al., 1999; Ono et al., 2001; Kato et al., 2005)

Actually, the meta analysis by Cao et al. (2009) compared clinical outcomes of ESD with EMR in the treatment of tumors of the gastrointestinal tract, they found that ESD showed better en bloc and curative resection rates and local recurrence, but was more time-consuming and had higher rates of bleeding and perforation complications. Lian et al. (2012) demonstrated that ESD is more promising, but it had the disadvantages of higher complication rates for perforation and bleeding.

The comparison between ESD and EMR in the treatment of early esophageal carcinoma is still controversial. Therefore, we designed the meta-analysis to systematically evaluate the two techniques, providing evidence for endoscopic treatment of early esophageal carcinoma. In the view of the present meta-analysis and all available trials, we suggest that ESD is appropriate to most of the lesions, the reason is that ESD has higher resection rate without increasing the procedure related complications.

In summary, based on the findings of our meta-analysis, ESD showed considerable advantages over EMR for early esophageal carcinoma regarding en bloc resection rate, histologically complete resection rate, and local recurrence even for small lesions, without increasing the procedure-related complication rate. Yet, more high quality trials including early esophageal carcinoma patient are needed to prove the effectiveness of ESD.

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